CERTIFICATE OF MAILING
37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date below:

March 25, 2002 — Date
Steven L. Highlander

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Ruth A. Gjerset

Serial No.: 09/556,440

Filed: April 24, 2000

For: DOWN-REGULATED OF DNA REPAIR TO ENHANCE SENSITIVITY TO P53-MEDIATED SUPPRESSION

Group Art Unit: 1642

Examiner: B. Brumback

Atty. Dkt. No.: INRP:032—2/SLH

DECLARATION OF DEBORAH R. WILSON, PH.D, UNDER 37 C.F.R. 1.132

Commissioner of Patents
Washington, D.C. 20231

I, Deborah R. Wilson, Ph.D, declare that:

1. I am the Associate Vice President of Clinical Research at Introgen Therapeutics, Inc. ("Introgen"), assignee of the above-captioned application. I have been employed at Introgen for 7 years and was recently named Associate Vice President. My responsibilities as Associate Vice President of Clinical Research at Introgen include clinical science, pharmacokinetics, and drug safety. I am a citizen of the United States of America, and I reside at 11022 Silkwood, Houston, Texas 77031.

2. I understand that the Patent and Trademark Office has rejected claims in the above-referenced case as lacking enablement, based on reasons related to the lack of success of gene therapy.

3. Introgen and its collaborators have been conducting research and development of an Ad-p53 composition for the treatment of cancer for at least 10 years. Introgen's research and development has progressed to the point where its Ad-p53 composition, INGN 201 (Introgen's Advexin® adenovirus p53 product), which is disclosed in the present application, is involved in a number of clinical trials for head and neck cancer, lung cancer, breast cancer, esophageal cancer, glioma, prostate cancer, advanced solid tumors, bladder cancer, and ovarian cancer. *See* Table of Adenovirus-p53 Clinical Trials (Exhibit 1). INGN 201 is in phase III clinical trials for head and neck cancer. Phase II clinical trials are underway or have been completed for head and neck cancer, esophageal cancer, breast cancer, and non-small cell lung carcinoma. INGN 201 was used or has been approved for phase I clinical trials for lung cancer, breast cancer, liver cancer, glioma, prostate cancer, head and neck cancer, bladder cancer, ovarian cancer, colorectal cancer, malignant ascites, and solid tumors from a variety of origins.

4. Several clinical trials have been conducted for various cancers including ovarian cancer, lung cancer, bladder cancer, and metastatic colorectal cancer using a different Ad-p53 construct from another company, Schering Plough.[1]

5. The clinical trials discussed in paragraphs 3 and 4 involved or will involve a variety of administrations of Ad-p53 constructs. Administrations include: intraperitoneal,

[1] *See, e.g.*, Barnard (2000); Horowitz (1999); Kuball *et al.* (2002); Schuler *et al.* (2001) and the reference of Wills *et al.*, which provides the details regarding the structure of the SCH 58500 Ad-p53 construct, which lacks protein IX. (Exhibit 2)

intravenous, intravesical, intratumoral, intramucosal injection, oral rinse, and broncho-alveolar lavage.

6. I anticipate Introgen will proceed with other clinical trials in the future involving adenovirus-p53 constructs, given the success I have observed in the ongoing or previous clinical trials with Introgen's product, INGN 201.

7. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under § 1001 of title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this patent, and any reexamination certificate issuing thereon.

_____ _____

Date Deborah R. Wilson, Ph.D.